



# Good Afternoon!

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# OLLI Fall 2020 Semester

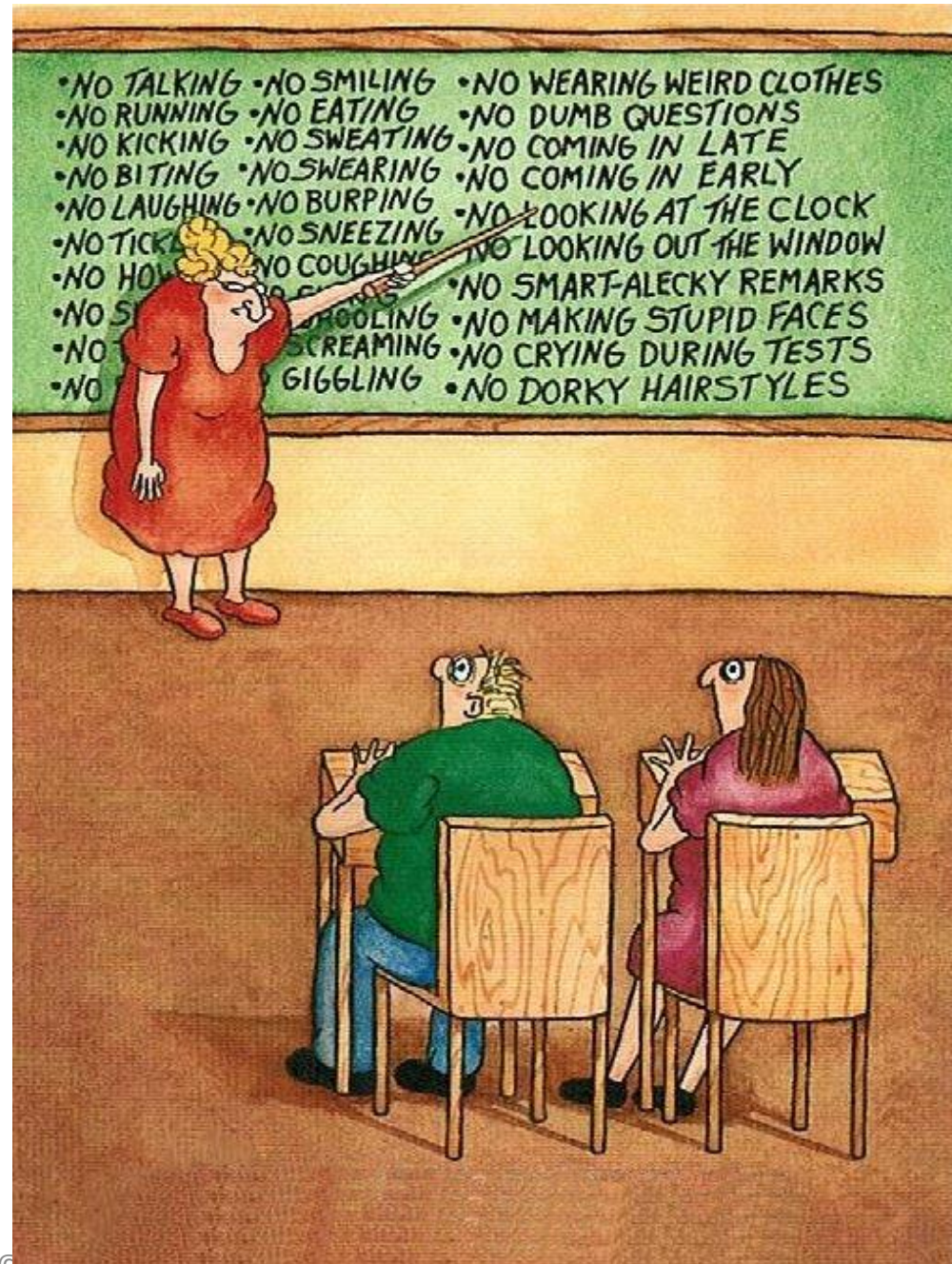
October 13, 2020

Néstor A. Ramírez, MD, MPH

The background of the slide features a pair of rich red, heavy curtains with deep folds and a scalloped top edge, framing a central white rectangular area. The curtains are pulled back slightly to reveal the white space where the text is located.

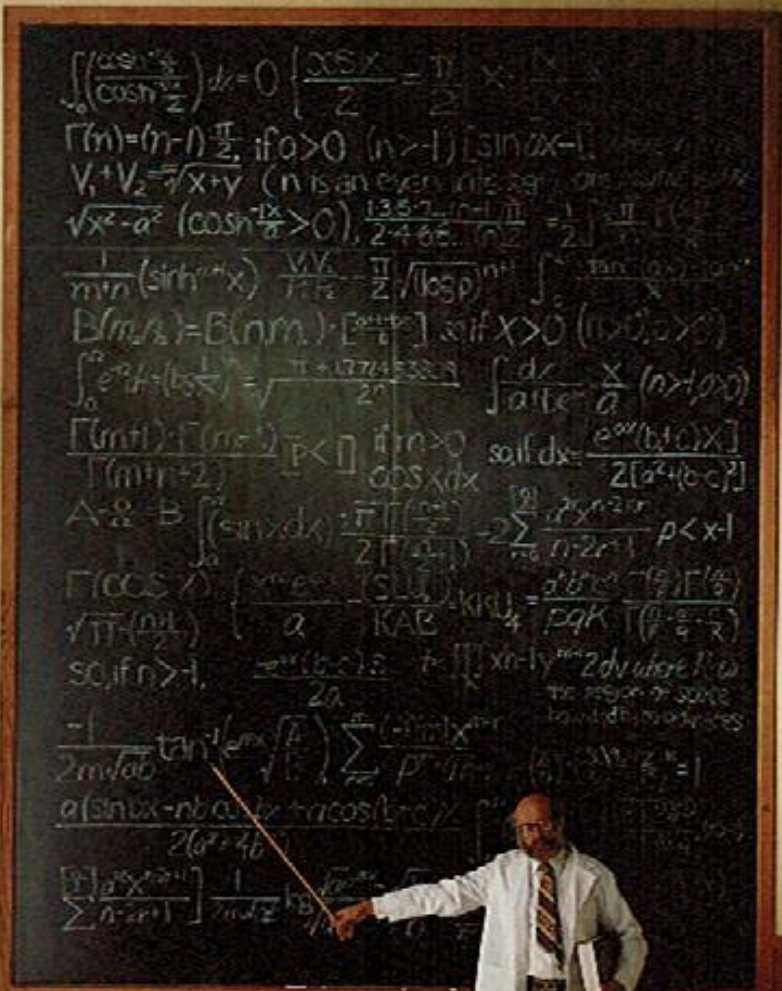
# **Plagues, Pestilences Poxes and Pandemics**

# Some Housekeeping Rules Before We Begin

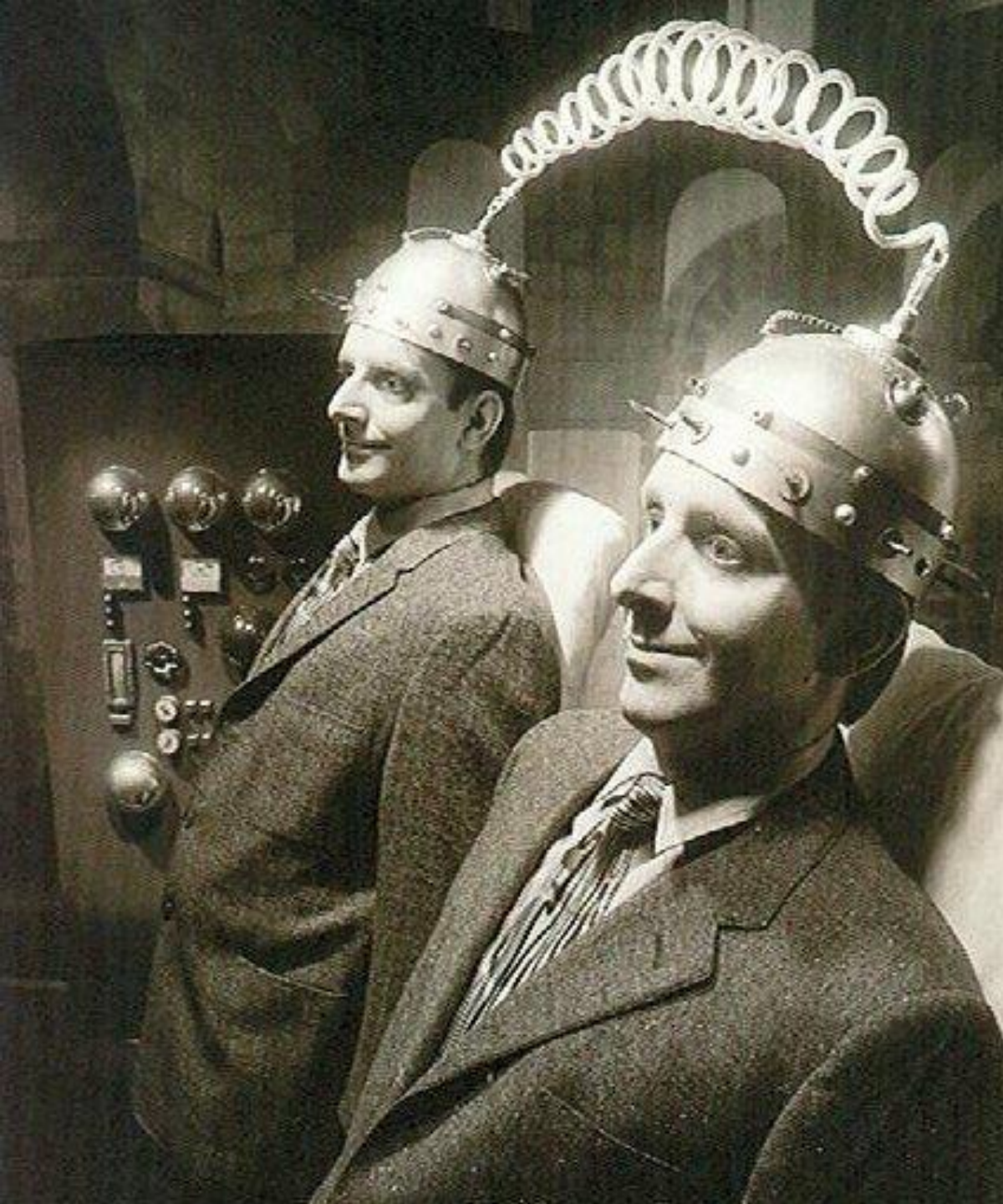


# Session 7

## 20<sup>th</sup> and 21<sup>st</sup> Century Viruses



I'll try to keep it simple!



Hope You Get  
a Charge  
From Today's  
Session!

# Alphabetical List of Some “Baddies”

- Borna
- Chikungunya\*
- Corona
- Dengue\*
- Ebola
- Hanta
- Hendra
- Herpes
- HIV
- Influenzas
- Junín
- Lassa
- Machupo
- Marburg
- MERS\*
- Nipah
- Noro
- Poxes
- SARS\*
- Sin Nombre
- West Nile\*
- Yellow Fever
- Zika



# For All the Viral Fevers

- Other Names
- Etiology
- Vector & Mechanism of Infection.
- Distribution & Incidence
- Incubation & Symptoms
- Complications & Mortality
- Treatment
- Prevention: Medical and Environmental

All of today's topics  
are related and very  
interconnected.



# ***FLAVIVIRUS* GENUS**

# Flavivirus

- *Flavus* = yellow in Latin.
- RNA viruses with arthropod vectors, cause of serious human diseases like yellow fever, dengue, West Nile, various types of encephalitis, and hepatitis C.
- Share several aspects:
  - Common size (40–65 nm).
  - Symmetry: enveloped, icosahedral nucleocapsid.
  - Single-stranded RNA positive-sense.
  - About 10,000–11,000 bases.
  - Similar appearance in the electron microscope.



# CHIKUNGUNYA

# Chikungunya

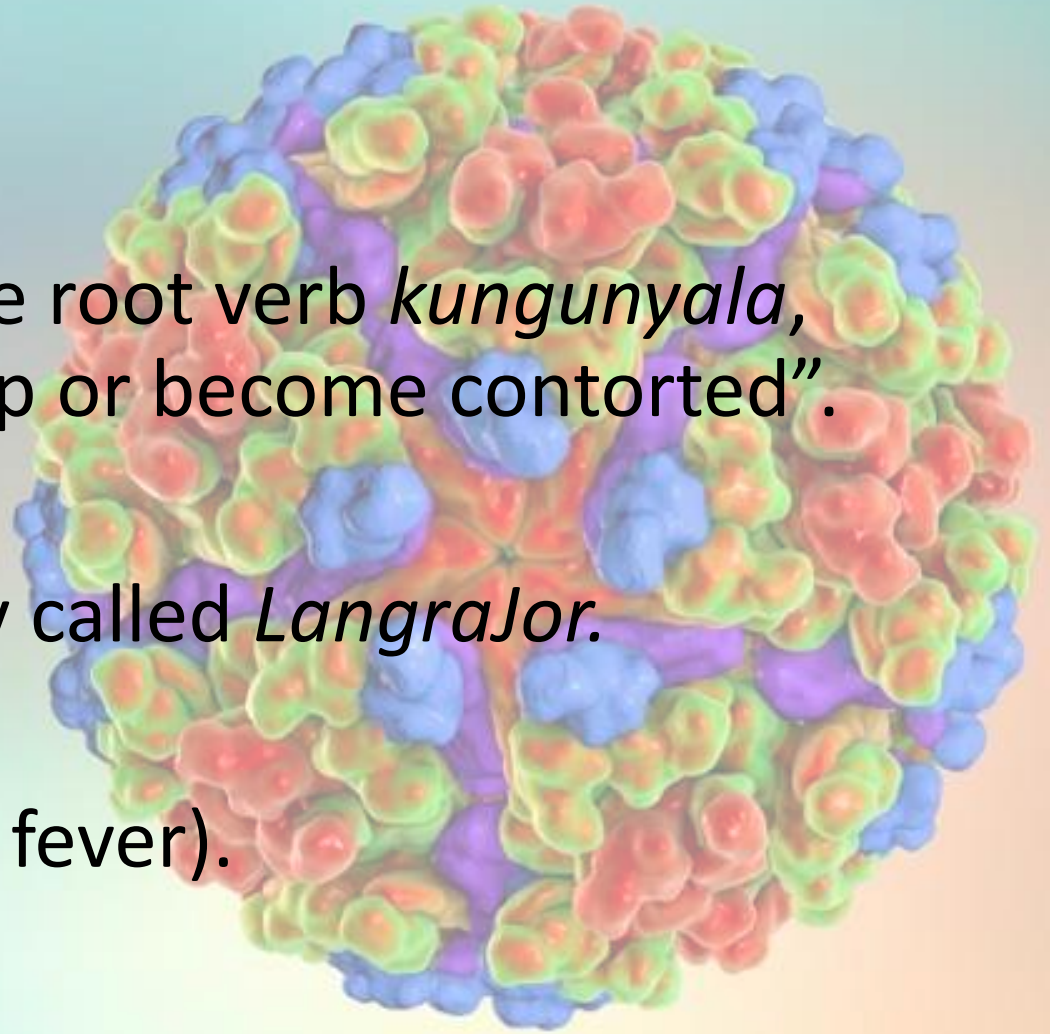


It has **NOTHING** to do with **Chickens** !

# Chikungunya

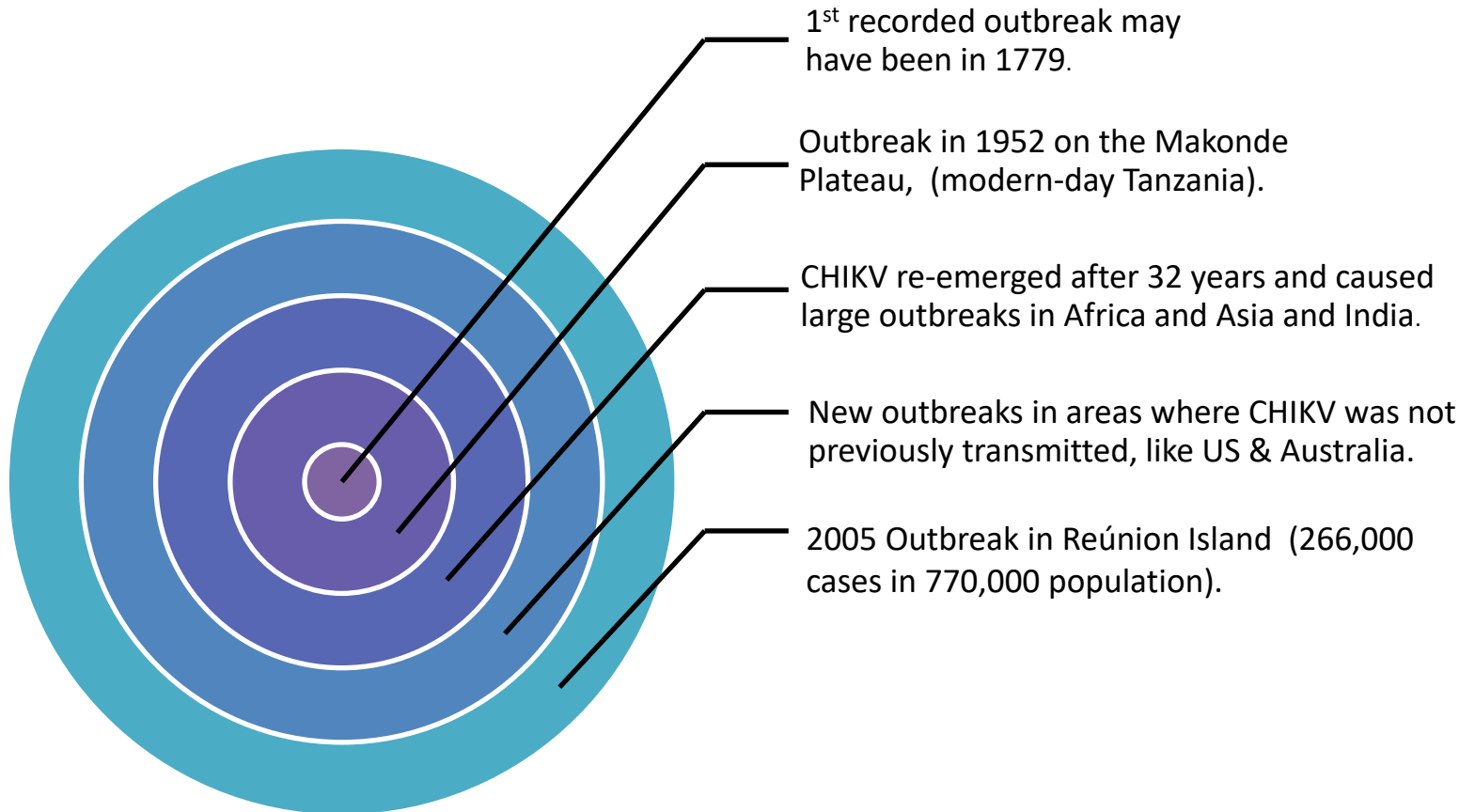
## Other Names

- CHIKV.
- From the Makonde root verb *kungunyala*, meaning “to dry up or become contorted”.
- In Tanzania, locally called *LangraJor*.
- Fiebre Chica (little fever).



# Chikungunya

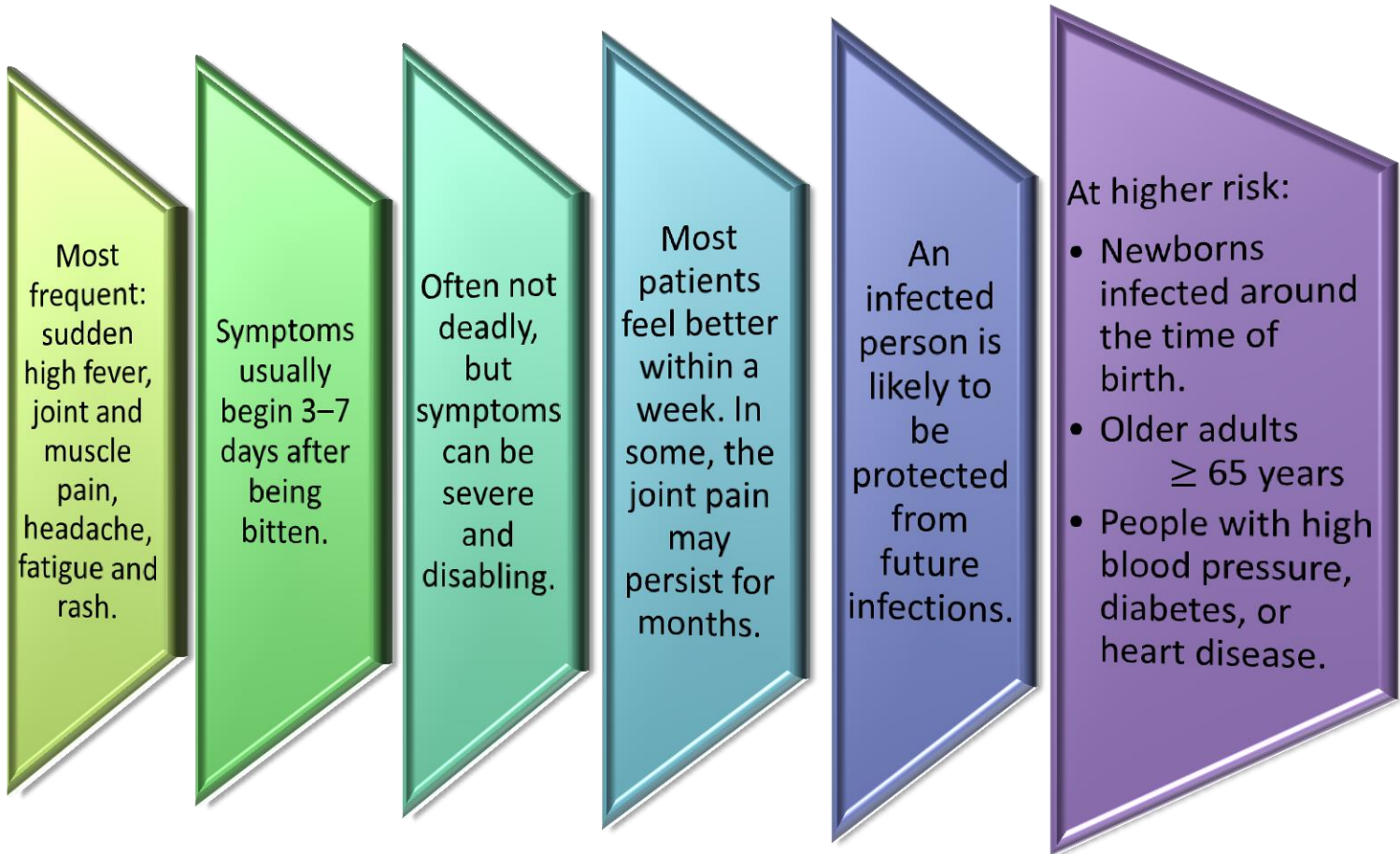
## Historical Perspective





# Chikungunya

## Signs & Symptoms



# Chikungunya

## Joint Pains (Arthralgias)



Joint stiffness, strong pains and rare swelling in 87-98% of cases.

Occur 2 to 12 days after exposure.

Joint pain may last for months or years.

Can be debilitating, with near immobility.

Joints are affected symmetrically in both arms and legs.

Pain most common in peripheral joints.

# Chikungunya

## Etiology & Mechanism of Infection <sup>(1)</sup>

- CHIKV is a single-strand RNA virus transmitted by an arthropod, *Aedes* mosquito.
- Arbovirus = **Ar**thropod **borne** virus.
- Mosquito bite injects saliva and sucks blood.
- Salivary glands of *Aedes* infected with CHIKV.

# Chikungunya



*Aedes aegypti*  
in the act of  
biting a  
human.

# Chikungunya

## Etiology & Mechanism of Infection (2)

- CHIKV injected by female *Aedes* mosquito.
- Males do not suck blood.
- In the 1<sup>st</sup> week CHIKV is found in the blood and can pass from a person to a mosquito.
- An infected mosquito can then spread the virus to other people.

# Chikungunya

## Viral Genetics

- Analysis of CHIKV genetic code suggests that the severity of the current outbreak may be due to a mutation in the viral coat protein.
- This allows the virus to multiply more easily in mosquito cells.
- This lets CHIKV to use the Asian tiger mosquito *A. albopictus* in addition to the tropical main vector, *Aedes aegypti*.
- *Ae. albopictus* is an invasive species which has spread worldwide.
- Increased outbreak risks where the Asian tiger mosquito is present.

# Chikungunya

Distribution (PAHO 2019)

- Outbreaks have occurred in Africa, Asia, Europe, and the Indian and Pacific Oceans.
- In late 2013, the virus was found for the first time on islands in the Caribbean.
- The virus may be imported to new areas by infected travelers.
- No human-to-human transmission: human-to-mosquito transmission (reverse zoonosis).

# Chikungunya

## Prevention

You can prevent mosquito bites:

- Wear light-colored long sleeves and pants.
- Stay in places with air conditioning.
- Be in rooms that use window and door screens.
- Use insecticide-impregnated bed net.
- Avoid strong perfumes.
- Use bug lightbulbs.
- Use insect repellent:
  - Ultrasonic clip-ons, smartphone apps (?)
  - Vitamin B1 tablets or patches (?)
  - Natural oils: clove, peppermint-castor oil, lemon-eucalyptus, lavender, neem.
  - Wristbands (?)



# Chikungunya

## Environmental Prevention

- Stop mosquitoes from laying eggs in or near water.
  - Once a week:
    - Empty and scrub:
    - Turn over:
    - Cover or throw out:
- Items that hold water, like tires, buckets, planters, toys, pools, birdbaths, flowerpots, or other containers.
- Check in and outdoors.

# Chikungunya

## Treatment

There is no specific medicine to treat chikungunya virus.

Treat the symptoms:

Do not take aspirin or other NSAIDS until dengue can be ruled out

If taking medicine for another medical condition, talk to your healthcare provider.

Get plenty of rest.

Drink fluids to prevent dehydration.

Take acetaminophen to reduce fever and pain.

# Dengue virus

## DENGUE

# Dengue Fever

## Other Names

Breakbone/Breakheart fever.

*E. Africa Kidinga pepo: a cramp-like seizure.*

Dandy fever.

Pasito Tun-Tun.

Philippine/Thai hemorrhagic fever.

## Etiology <sup>(1)</sup>

Bite of infected mosquito.

Single bite can infect.

Infected blood products.

Organ transplants.

Sexual transmission (rare).

Mother to baby: pregnancy or childbirth.

# Dengue Fever

## Etiology <sup>(2)</sup>

Single strand  
linear  
positive  
sense RNA.

*Flavivirus*  
genus (flavus  
= yellow).

Viral genetic  
variation is  
region-  
specific.

Infection with  
1 strain gives  
life-long  
immunity

Same family  
as yellow  
fever, Zika &  
West Nile.

Humans  
primary host,  
also other  
primates.

Minimal  
immunity to  
other 2  
strains.

2<sup>ary</sup> infection  
by other strain  
increases risk  
of severe  
disease.

# Dengue Fever

## Etiology <sup>(3)</sup>

Larval stages are found in water-filled habitats associated with human dwellings, often indoors.



Dengue virus transmitted through the bite of an infective female *Aedes*.



Virus infects the mosquito mid-gut and then the salivary glands over 8-12 days incubation.



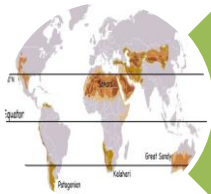
After this time, virus can be transmitted to humans during subsequent probing or feeding.

# Dengue Fever

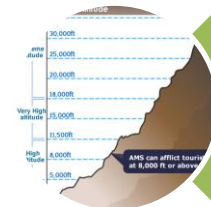
## The Vector (1)



*Aedes*, from the Greek “unpleasant, odious.”  
(*Aedes aegypti*, *albopictus* and *polynesiensis*.)



Between Lat. 35° North and 35° South.



Elevation < 3,300 ft.



May bite at any time of day.

(Prefer early morning and evening.)

# Dengue Fever

## The Vector (2)

Dengue infection rates are higher outdoors and during daytime, when the *Aedes (Stegomyia) albopictus* bite most frequently.

*Ae. albopictus* is primarily a forest species that has become adapted to rural, suburban and urban human environments.

In last 40 years *Ae. albopictus* has spread from Asia to Africa, the Americas and Europe, via the international trade in used tires.

The eggs can withstand very dry conditions and remain viable for many months in the absence of water.

*Ae. aegypti* breed indoors and can bite all day.

Indoor habitat increases the mosquitoes' longevity.

Females may spend their lifetime in or around the houses where they became adults.

Usually fly at most 1,200 feet, so it's people that rapidly move the virus within and between places.



# Dengue Fever

## The Vector <sup>(3)</sup>

- In March 2019, a study found that the song "Scary Monsters and Nice Sprites" by Skrillex delays host attack, *blood feeding*, and *disrupts the mating process of Aedes aegypti*.
- This research opens new avenues for the development of music-based personal protective and control measures for mosquitoes.
- The research involved that song only, not the influence of different ones.

# Dengue Fever

## Distribution & Incidence

Common in more than 120 countries.

In 2013: ~ 60 M symptomatic infections worldwide, with 18% hospitalizations and about 13,600 deaths.

Worldwide cost of dengue is estimated at US \$9 B. per year.

12 countries in SE Asia estimated to each have ~ 3 M infections and 6,000 deaths annually.

In 2019 the Philippines declared a National Dengue Epidemic due to 622 deaths that year.

In >22 countries in Africa, 20% of population at risk.

# Dengue Fever

## Symptoms

- 80% are asymptomatic or have only mild symptoms.
- 5% have more severe illness; in a small portion it is life-threatening.
- The incubation period is 3 to 14 days, average 4 to 7.
- if symptoms start >14 days after arriving home, travelers returning from endemic areas are unlikely to have dengue

# Dengue Fever

- 80% have benign course with headache, prostration, fever, severe joint & muscle pain, lymphadenopathy and rash.
- The "dengue triad" of fever, rash, and behind-the-eyes headache is characteristic.
- 1 to 5 % of patients get severe dengue (known as dengue hemorrhagic fever, DHF).
- Blood vessels leak, patients bleed from their gums and under the skin; 20% percent may die.
- Half of them get DSS (dengue shock syndrome) with severe hypotension.

# Dengue Fever

## Symptoms in Children

- Children have symptoms like the common cold and gastroenteritis (vomiting and diarrhea).
- They have more risk of severe complications.
- Initial symptoms are generally mild but include high fever.
- **More pronounced in well-nourished children!**

# Dengue Fever

## Dengue Hemorrhagic Fever and Dengue Shock Syndrome

Spread of dengue post WWII attributed to ecologic disruption.

Also led to different disease serotypes into new areas and the emergence of DHF and DSS.

DHF and DSS first noted in Central and South America in 1981, becoming a major cause of child mortality.

**People who had been infected with DENV-1 several years earlier now had DENV-2.**

# Dengue Fever

## Prevention

- Prevention is similar to other arboviruses:
  - Eliminate the vector's habitats.
  - Drain stagnant water.
  - Animals which eat the larvae: guppies, copepods.
  - Spray mineral oil on still waters to choke larvae.
- Insecticides & larvicides (dunks) may be toxic.
- GM males that produce non-flying offspring.
- Bacteria to infect the mosquito (*wolbachia*).

# Dengue Fever

## Larvae in Water



Caudal appendage (“periscope”) to absorb oxygen.

Other non-toxic tips to eliminate larvae:

Cinnamon oil

Apple cider vinegar

Aerators

Decrease surrounding vegetation

Soapy water



# Questions?



# WEST NILE

# West Nile Virus Distribution



# West Nile Virus

## Etiology

- Single strand, positive sense RNA flavivirus.
- In the antigenic serocomplex of Japanese encephalitis, with Murray Valley , Saint Louis, Venezuelan equine and other encephalitis.
- Phylogenetic studies have shown that WNV emerged as a distinct virus ~1000 years ago.
- Rarely spread through transfusions, organ transplants, or from mother to baby during pregnancy, delivery, or breastfeeding.
- Unlike in birds, it does not spread directly between people.

# West Nile Virus in USA (1)



1999



2000



2001



2002



2003



2004



2005

Cases in a year

White: 0%

Blue: <1%

Green: 1%

Yellow: 5% to 10%

Red: >10%

# West Nile Virus in USA (2)

- 1999: 62 cases, 7 deaths, mostly NYC & 4 states.
- 2000: 21 cases, 2 deaths.
- 2001: 50 cases, 5 deaths.
- 2002 hot & dry summer July to Oct. 38 states:
  - Illinois: 714 cases, 45 deaths.
  - Michigan: 463 cases, 36 deaths.
  - Louisiana: 317 cases, 16 deaths.
- 2012: 5,674 cases, 286 deaths.
- 2015: 2,175 cases, 146 deaths

# West Nile Virus in USA (2)

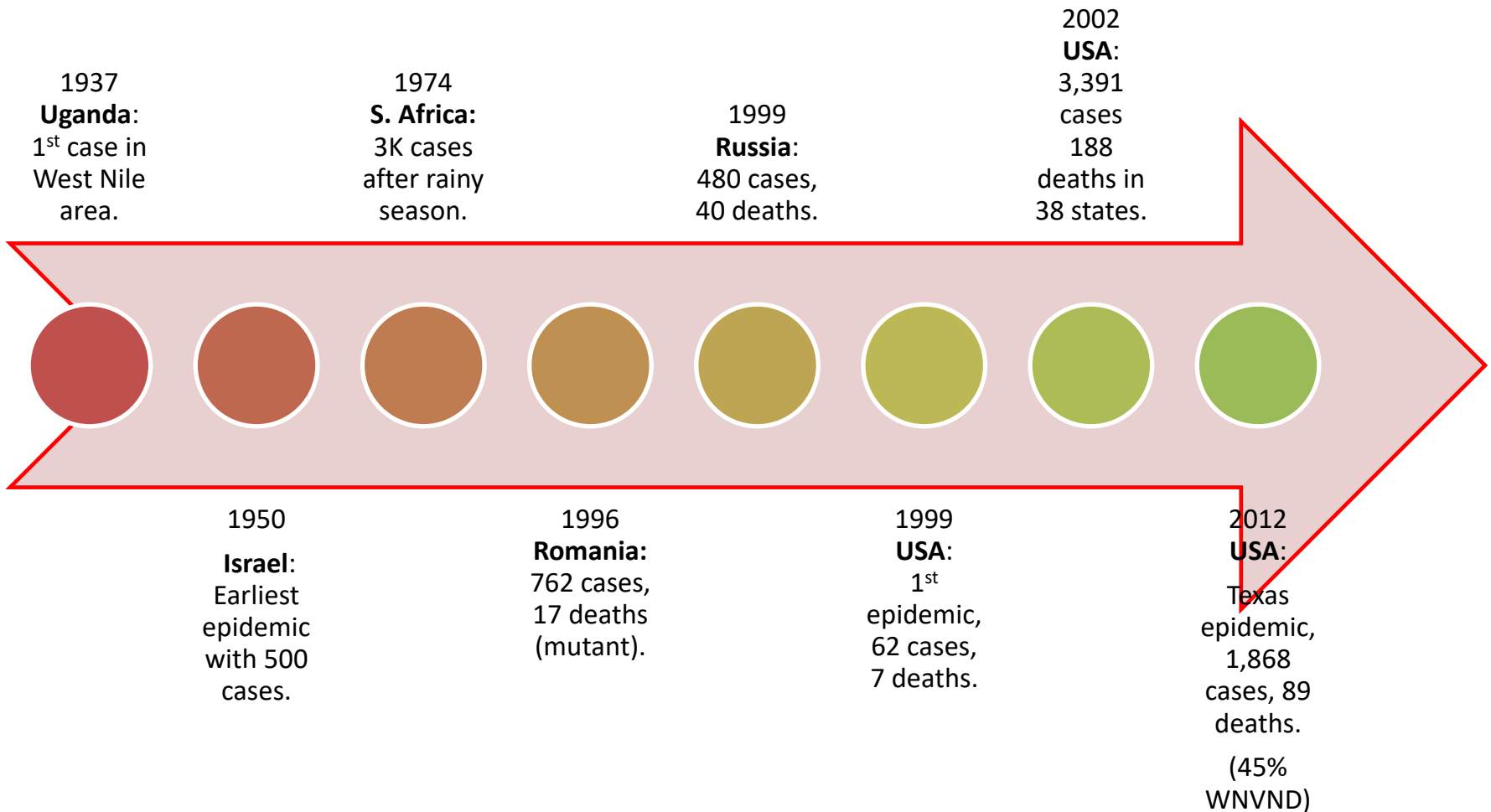
Year	Cases	Death	%
1999*	62	7	11
2000*	21	2	10
2001*	66	10	15
2002	4,156	284	7
2003**	9862	264	3
2004	2539	100	4
2005	3,000	119	4
2006	4,269	177	4
2007	3,623	124	3
2008	1,356	44	3
2009	720	57	4

Year	Cases	Deaths	%
2010	1,021	57	6
2011	712	43	6
2012**	5,674	286	5
2013	2,469	119	5
2014	2,205	97	4
2015	2,175	146	7
2016	2,149	106	5
2017	2,097	146	7
2018	2,647	167	6
2019	958	54	6
2020	?	?	?

CDC 2019

# West Nile Virus

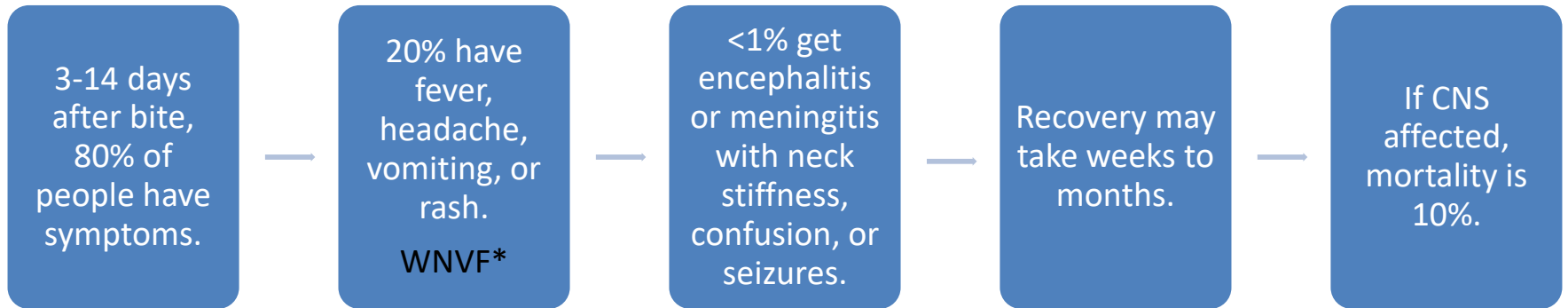
## WNV Timeline





# West Nile Virus

## Incubation & Symptoms



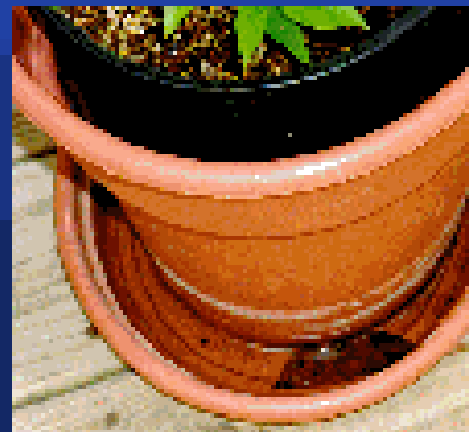
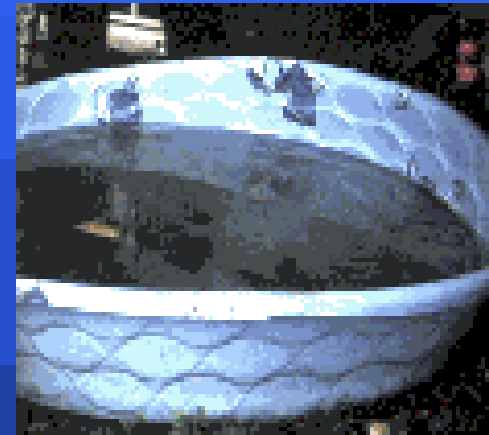
WNVF: mild flu-like symptoms.

# West Nile Virus

## Prevention

- No vaccine for humans (but yes for horses).
- Reduce infection risk by avoiding mosquito bites.
- Eliminate standing pools of water, like old tires, buckets, gutters, and swimming pools.
- Mosquito repellent, window screens, and mosquito nets reduce the risk of being bitten.

# Mosquito Breeding Sites



# West Nile Virus

## Treatment

- No specific treatment.
- Treat symptomatically.
- Treat complications, especially CNS.
- Prevention is your best treatment.

# West Nile Virus

## WN Virus Complications

- Neuroinvasive Disease (WNVND) <1% :
  - Encephalitis (WNE).
  - Meningitis (WNM).
  - Poliomyelitis (WNP).
- Non-neurologic complications:
  - Fulminant hepatitis and/or pancreatitis.
  - Myocarditis or cardiac dysrhythmias.
  - Rhabdomyolysis.
  - Orchitis, nephritis.
  - Skin rashes.
  - Optic neuritis or chorioretinitis.
  - Hemorrhagic fever with coagulopathy.

# West Nile Virus

## Vector & Mechanism of Infection

- Mosquitoes of the genus *Culex*:
  - *Pipiens*: Eastern US, urban areas north of 36-39°N.
  - *Tarsalis*: Midwest and West.
  - *Quinquefasciatus*: Southeast.
- WNV vectors prefer members of the thrush family like the American crow and the American robin.
- Infected mosquito bites a healthy bird, the virus amplifies within the bird, an uninfected mosquito bites the bird and now the mosquito is infected.
- Bird may die gradually or suddenly in 10-14 days.

# West Nile Virus Transmission Cycle

*Reservoir Hosts*  
Birds

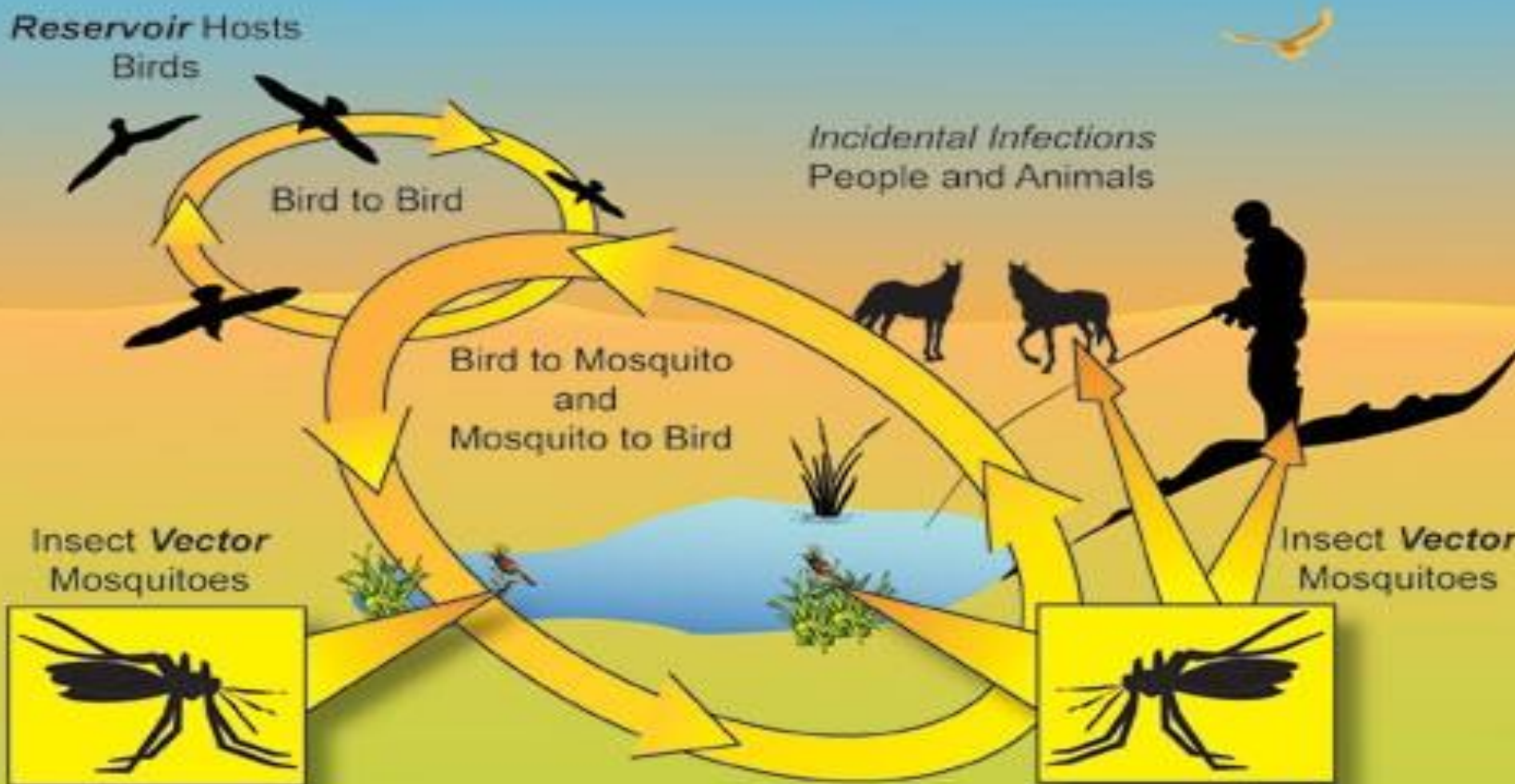
Bird to Bird

*Incidental Infections*  
People and Animals

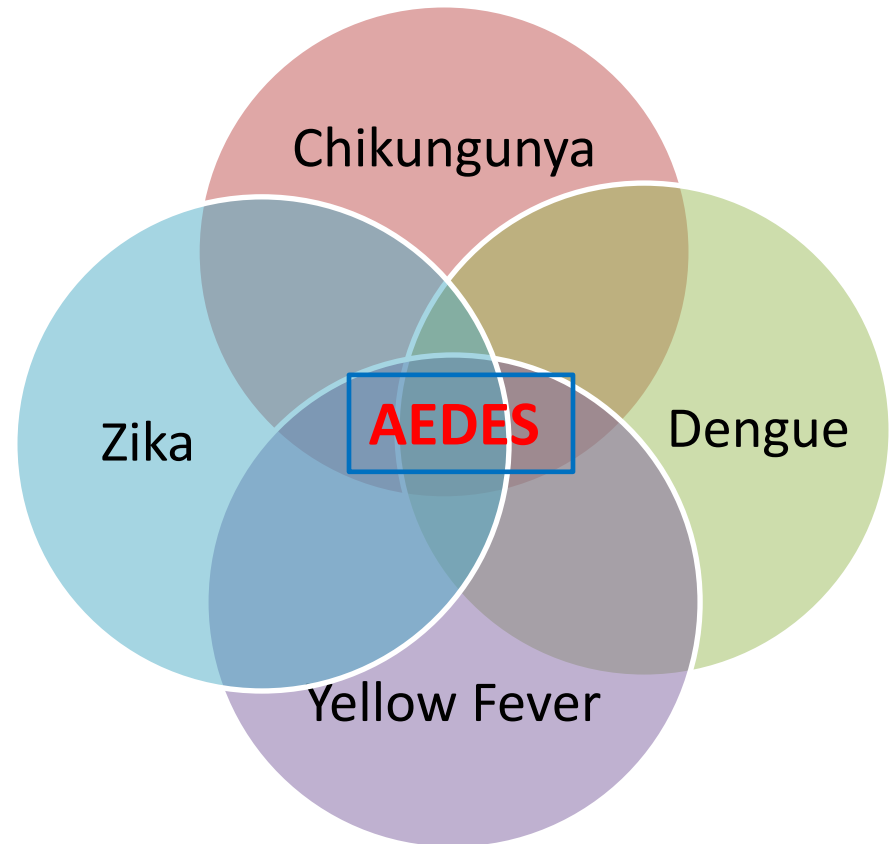
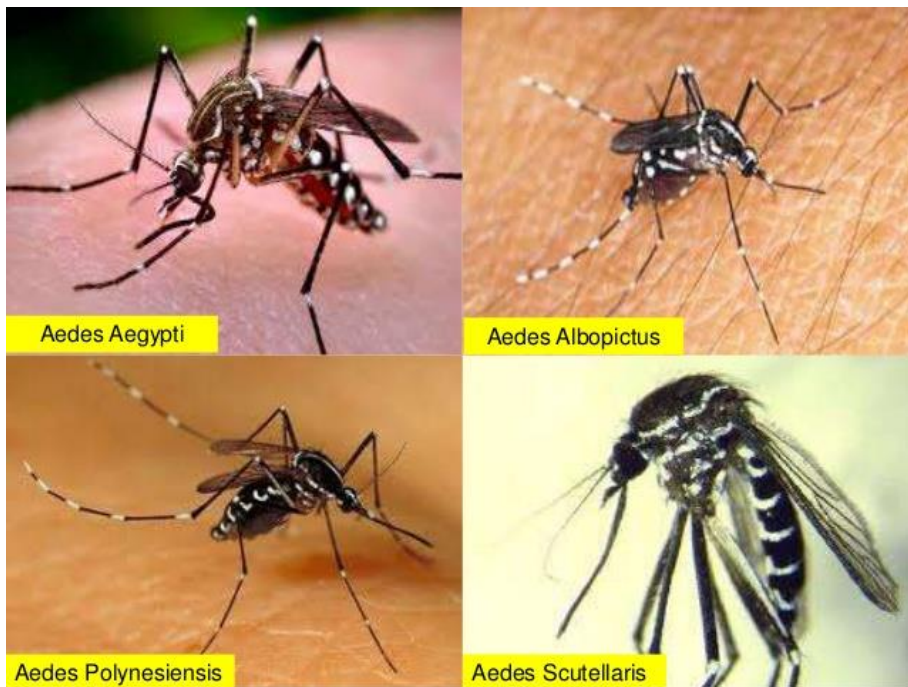
Bird to Mosquito and  
Mosquito to Bird

*Insect Vector*  
Mosquitoes

*Insect Vector*  
Mosquitoes



# The *Aedes* Vector Superfecta





# Those Pesky Mosquitoes!





# MOSQUITOES CAUSE MORE DEATH & DISEASE THAN ANY OTHER ANIMAL ON THE PLANET

MALARIA DENGUE FEVER YELLOW FEVER  
JAPANESE ENCEPHALITIS WEST NILE VIRUS  
CHIKUNGUNYA FEVER KUNJIN VIRUS  
JAMESTOWN CANYON VIRUS  
VENEZUELAN EQUINE ENCEPHALITIS  
ST. LOUIS ENCEPHALITIS POGOSTA DISEASE  
ROSS RIVER VIRUS LYMPHATIC FILARIASIS  
EASTERN EQUINE ENCEPHALITIS  
MURRAY VALLEY ENCEPHALITIS  
RIFT VALLEY FEVER LA CROSSE ENCEPHALITIS

# Corona Viruses

Related strains:  
SARS, MERS, COVID-19

# SARS

# CORONA VIRUSES (1)

## SARS

- Severe acute respiratory syndrome (SARS) is a zoonotic origin virus called SARS-CoV or SARS-CoV-1.
- Caused the 2002–2004 SARS outbreak.
- In 2017, Chinese traced the virus through Asian palm civets to cave-dwelling horseshoe bats in Yunnan.
- At end of the epidemic in June 2003, the incidence was 8,422 cases with a case fatality rate (CFR) of 11%.

No cases of SARS-CoV have been reported since 2004.

# CORONA VIRUSES (2)

## SARS

- Flu-like symptoms: fever, muscle pain, lethargy, cough, sore throat, diarrhea and other nonspecific symptoms.
  - Common to all patients is a fever above 100 °F.
  - May lead to shortness of breath and pneumonia; either viral or secondary bacterial pneumonia.
- Average incubation is 4–6 days (range 1 to 14).
  - Transmission is through respiratory droplets or fomites.
  - $R_0$  ranges from 2 to 4 depending on different analyses.
  - Control measures in April 2003 reduced  $R_0$  to 0.4.



# Corona Viruses <sup>(4)</sup>

## SARS Treatment

- Symptomatic only.
- Antibiotics only for 2<sup>nd</sup>ary bacterial infections.
- Antivirals like ribavirin, lopinavir, ritonavir, type I interferon, have not been useful.
- British recommend corticosteroids in severely ill patients with O<sub>2</sub> saturation of <90%.
- No vaccine available.



# MERS

# CORONA VIRUSES (5)

## MERS Other Names

- Middle East Respiratory Syndrome.
- Also called the “Camel flu”.
- Sometimes Saudi Arabia’s SARS-like virus.
- MERS-CoV is a single strand coronavirus believed to come originally from bats.

# CORONA VIRUSES (6)

## MERS Symptoms

- Caused by MERS-coronavirus (MERS-CoV).
- Symptoms: none to mild to severe:
  - Fever: 98%.
  - Cough: 83%.
  - Diarrhea: 26%, vomiting 21%, abdominal pain 17%.
  - Shortness of breath (SOB): 72%.
  - Myalgia: 32%.
- 72% required mechanical ventilation.

# CORONA VIRUSES (7)

## MERS Symptoms & Complications

- Incubation of 5.5 days (range 2 to 15).
- High incidence of severe pneumonia and respiratory failure.
- ECMO useful in improving outcomes.
- Neither combination of antivirals and interferons nor corticosteroids improved outcomes.

# CORONA VIRUSES (8)

## MERS Transmission (a)

- Unclear how virus goes from camels to humans.
- WHO advises:
  - Avoiding contact with camels.
  - Eating only fully cooked camel meat.
  - Drinking only pasteurized camel milk.
  - Avoid drinking camel urine.
- Limited evidence of spread of MERS-CoV from person to person in households and in hospitals, but no evidence of transmission from asymptomatic cases.

# CORONA VIRUSES <sup>(9)</sup>

## MERS Transmission <sup>(b)</sup>

- Humans are typically infected from camels, either during direct contact or indirectly.
- Saudi Ministry of Agriculture advises wearing masks when around camels.
- Some people have refused to listen to the government's advice and kiss their camels in defiance.

# CORONA VIRUSES (10)

## MERS Symptoms

- First case in June 2012 in Saudi Arabia.
- Most cases have occurred in the Arabian Peninsula.
- ~2,500 cases have been reported as of January 2020.
- About 35% of those diagnosed die from it.
- Large outbreaks have occurred in South Korea in 2015 and in Saudi Arabia in 2018.

# Summary

Virus	Vector	Treatment	Vaccine	Fatality
CHIKV	Aedes	Symptomatic	No	0.1%
Dengue	Aedes	Symptomatic	T2	10%
MERS	Camel	Symptomatic	No	35%
SARS	Rat/Civet?	Symptomatic	No	11%
West Nile	Culex	Symptomatic	No	3-15%



# We Are at the Cusp!







